

# Clinical value of the *Treponema pallidum* haemagglutination test

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The haemagglutination test, utilizing pathogenic *Treponema pallidum*, for the serological investigation of syphilis, was developed by Rathlev (1967) and provides the clinician with a test of high specificity and sensitivity. Commercially available reagents from Japan have been evaluated clinically by Uete, Fukazawa, Ogi, and Takeuchi (1971) and a similar haemagglutination test, using fowl erythrocytes, has been investigated by Sequeira and Eldridge (1973). Their results have confirmed that the haemagglutination test combines high sensitivity with high specificity in treated and untreated syphilis, except in some cases of early syphilis. With the late appearance of the antibody and its persistence after treatment, the *Treponema pallidum* haemagglutination test (TPHA) appears to share the advantages and, to a lesser extent, the disadvantages of the *T. pallidum* immobilization test.

This report is based on the results of an application of the TPHA test, using the commercial reagents from Japan, to the serological investigation of patients attending the Sexually-Transmitted Disease (STD) Department of the Royal Infirmary of Edinburgh (R.I.E.) during the first part of 1973 (Young, Henrichsen, and Robertson, 1974). In all cases showing positive reactions, even very weakly positive reactions, the fluorescent treponemal antibody absorbed (FTA-ABS) test was carried out.

## Patients investigated

From February 20 to May 8, 1973, a total of 1,129 individual patients (697 males and 432 females) attended the STD Department at the R.I.E. As part of the investigations on these patients, serological tests to exclude syphilis were performed. In addition the same tests were carried out on 65 patients treated previously for syphilis (with penicillin).

## Methods

The serological tests comprised the venereal disease research laboratory (VDRL) slide test and the Reiter

protein complement-fixation (RPCF) test in addition to the TPHA test using the commercial reagents supplied by the Fuji-zoki Company, Tokyo, Japan. The FTA-ABS test was available when necessary. The methods used, including that in the quantitative TPHA test, were the same as described previously (Young, Henrichsen, and Robertson, 1974).

## Results

### PATIENTS ATTENDING THE STD DEPARTMENT

(1) *Cases of syphilis discovered by VDRL and/or RPCF test and confirmed by positive FTA-ABS or by the finding of T. pallidum in a genital sore by dark-ground examination*

Of the 1,129 patients, six cases of syphilis (Table I) were detected by the VDRL test and two of these were found to have a positive RPCF test. In two of the primary cases of syphilis the TPHA test was negative and in another female patient under surveillance after contact with a patient with early syphilis, the TPHA test did not become positive before changes were detected by the FTA-ABS and the VDRL test (Case B2).

(2) *Cases of syphilis discovered by the TPHA test and confirmed by the FTA-ABS but not detected by the VDRL and/or the RPCF test*

Of the 1,129 patients, a further six cases of syphilis belonged to this category (Table II). These cases would not have been discovered by the VDRL or RPCF tests. Three of the six patients were merchant seamen; they admitted previous sexually-transmitted disease such as gonorrhoea, venereal warts, or non-specific urethritis, but denied a previous history of syphilis.

(3) *Cases discovered by the TPHA test but negative by the FTA-ABS, VDRL and RPCF tests*

Of the 1,129 patients examined, there were seven whose TPHA reaction was positive without other evidence of previous or developing syphilis. The TPHA reaction in relation to these patients is dealt with in detail in our earlier report (Young and others, 1974).

**TABLE I** Cases discovered by the VDRL and/or RPCF tests and confirmed by a positive FTA-ABS or by the finding of *T. pallidum* in a genital sore

Case no.	Sex	Age (yrs)	Test				Form of syphilis	Comment
			VDRL (Reciprocal of titre)	RPCF (Reciprocal of titre)	TPHA (Reciprocal of titre)	FTA-ABS		
A1	M	27	Positive (2)	Negative	Positive (2,560)	Positive	Primary	DG negative for <i>T. pallidum</i>
A2	M	38	Positive (4)	Negative	Negative	Positive	Primary	DG positive for <i>T. pallidum</i>
A3	M	35	Positive (64)	Positive (160)	Negative	Positive	Primary	DG positive for <i>T. pallidum</i>
A4	M	56	Positive (2)	Negative	Positive (80)	Positive	Latent	
B1	F	63	Positive (Neat serum)	Positive (10)	Positive (80)	Positive	Latent	
B2	F	42	Weak positive	Negative	Negative	Negative became positive 7 days later	Early	Sexual contact of patient with <i>T. pallidum</i> in genital sore

DG = Dark-ground examination of serum from lesion.

**TABLE II** Cases discovered by the TPHA test and confirmed by the FTA-ABS test but not detected by VDRL and/or RPCF tests

Case no.	Sex	Age (yrs)	Diagnosis	Test	
				TPHA (Reciprocal of titre)	FTA-ABS
A5	M	63	Congenital syphilis first treated with arsenicals and bismuth 49 years ago and with penicillin 12 years ago	Positive (320)	Positive
A6	M	25	Latent syphilis in seaman with history of other sexually-transmitted disease	Positive (80)	Positive
A7	M	26	Latent syphilis in seaman with history of other sexually-transmitted disease	Positive (640)	Positive
A8	M	34	Latent syphilis in seaman with history of other sexually-transmitted disease	Positive (160)	Positive
A9	M	69	Latent syphilis with previous risks of other sexually-transmitted disease	Positive (160)	Positive
A10	M	34	Probably latent syphilis No history of sexually-transmitted disease Patient defaulted	Very weak positive	Positive

#### PATIENTS TREATED PREVIOUSLY FOR SYPHILIS

In none of the 25 cases of penicillin-treated early syphilis (nine seropositive primary, seven secondary, and nine early latent) had the TPHA test become negative. Even in cases examined 20 years or more after treatment, the TPHA remained positive in all cases. The titres found in the tests are indicated in Table III.

Similarly, in none of the forty cases of penicillin-treated late syphilis (28 latent, one cardiovascular, eight neurosyphilis, and three congenital) was the TPHA negative after treatment (Table IV). Among the forty cases of late syphilis a titre of 1/640 was found in nineteen.

#### Discussion

In 1,129 individual patients attending the STD Department, a diagnosis of syphilis, confirmed in all

by the FTA-ABS test, was made in twelve (1 per cent.). In six of these patients (0.5 per cent.) syphilis was discovered by the TPHA test and would not have been detected by the VDRL and/or RPCF tests. The TPHA test, therefore, doubled the detection rate of syphilis.

In one patient with a healing primary sore, the TPHA was positive. In two other cases of primary syphilis the TPHA test was negative and in one patient examined during the incubation period the VDRL and FTA-ABS tests became positive before any changes were detected in the TPHA.

The TPHA had not become negative in any of the cases of treated syphilis. There was considerable variation in the TPHA titre in cases of treated syphilis. Statistically there was no significant relationship ( $P > 0.1$ ) between the titre found and the length of the interval after treatment for late syphilis, and there were insufficient data to enable

TABLE III *TPHA titres in 25 cases of treated early syphilis*

Type of syphilis	No of patients	Interval between treatment and TPHA test	Reciprocal titre						
			80	160	320	640	1,280	2,560	5,120
Seropositive primary	0	0-6 mths							
	2	7-12 mths	1				1		
	2	13 mths-2 yrs	1				1		
	1	3-5 yrs			1				
	2	6-20 yrs		1			1		
	2	More than 20 yrs	1			1			
Secondary	0	0-6 mths							
	1	7-12 mths				1			
	2	13 mths-2 yrs				1	1		
	2	3-5 yrs	1				1		
	2	6-20 yrs	1						1
Early latent	2	0-6 mths					1	1	
	2	7-12 mths						1	
	2	13 mths-2 yrs				2			1
	1	3-5 yrs				1			
	2	6-20 yrs	1			1			

TABLE IV *TPHA titres in 40 cases of treated late syphilis*

Type of syphilis	No of patients	Interval between treatment and TPHA test	Reciprocal titre						
			80	160	320	640	1,280	2,560	5,120
Latent	3	0-6 mths			1	1			1
	4	7-12 mths				2	1	1	
	1	13 mths-2 yrs				1			
	8	3-5 yrs		1		5	2		
	9	6-20 yrs			1	6	2		
	3	More than 20 yrs		1		1		1	
Cardio-vascular	1	2 yrs						1	
Neuro syphilis	1	0-6 mths		1					
	2	2-5 yrs			1			1	
	4	6-20 yrs			1	1	1		1
	1	More than 20 yrs				1			
Congenital	1	3 yrs			1				
	2	More than 20 yrs		1		1			

conclusions to be drawn about the relationship in early cases. More information is required concerning the TPHA titre in untreated syphilis.

The TPHA test is of undoubted value in the detection of syphilis beyond the very early stage. Unexplained positive reactions can occur, however, so that positive results in the TPHA only should be confirmed by another specific test such as the FTA-ABS before a firm diagnosis is made.

In screening for early syphilis the VDRL test is very important and should be repeated over a period of at least 3 months. In special cases, such as in contacts of infectious syphilis, the FTA-ABS test should be carried out. The normal practice of making dark-ground examinations in patients with lesions is, of course, also essential.

### Summary

In 1,129 patients attending the Department for Sexually Transmitted Diseases, the serum was

examined by three screening tests (VDRL slide, RCF, and TPHA) and twelve cases of syphilis (1 per cent. of patients attending the clinic) were discovered.

Six of these patients were considered to have latent syphilis (5 acquired, 1 congenital) and were detected only by the TPHA; all six cases were confirmed by the FTA-ABS.

The TPHA failed to detect three of the remaining six cases (2 primary and 1 very early, the latter in a contact of a patient with primary syphilis). All six cases were, however, detected by the VDRL.

In seven cases, the TPHA was positive in the absence of other evidence of present or previous syphilis. In these cases the FTA-ABS was also negative. The clinical application of the TPHA test in the detection of syphilis is discussed.

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## References

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 YOUNG, H., HENRICHSEN, C., and ROBERTSON, D. H. H. (1974) *Ibid.*, **50**, 341

## Une estimation de la valeur clinique du test d'hémagglutination du tréponème pâle

### SOMMAIRE

Les sérums de 1129 consultants du département des maladies sexuellement transmises furent examinés par

trois épreuves de triage (VDRL sur lame, RPCF et TPHA) et l'on découvrit 12 cas de syphilis (1 pour cent des consultants de la clinique).

Six de ces malades furent considérés comme atteints de syphilis latente (5 acquises, 1 congénitale) et ne furent reconnues que par le TPHA; tous les six cas furent confirmés par le FTA-ABS.

Le TPHA ne reconnut pas trois des six cas restants (2 primaires, 1 très précoce, le dernier étant un contact d'un malade atteint de syphilis primaire). Tous ces six cas furent cependant détectés par le VDRL.

Dans sept cas, le TPHA fut positif en l'absence d'autres preuves de syphilis actuelle ou antérieure. Dans ces cas, le FTA-ABS fut négatif également. On discute de l'application de l'épreuve TPHA dans la détection de la syphilis.